

Changes to the International Regulatory Environment

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Abstract

Since 2010, two significant international regulations regarding medical device development have come into force, the amendment to the European Union (EU) Medical Device Directive (MDD) 2007/47/EC and the United States (US) Food and Drug Administration (FDA) Final rule on Medical Device Data Systems (MDDS). Adherence to these regulations is mandatory to be able to market a medical device in the respective region. The ability to understand these regulations and apply them to a development project can be difficult. The MDDS final rule changes the safety classification of a number of devices from Class III-high risk to Class I-low risk. The aim of this regulation is to make the process of achieving regulatory approval for manufacturers easier. The MDD aims to provide guidance for the development of medical devices to be marketed for use within the EU. It also provides defined pathways which manufacturers can follow in order to achieve regulatory approval. However, changes made as part of amendment to the directive have a direct impact on the development of medical devices. One of the most significant changes as part of this amendment is for software to potentially be considered as a medical device in its own right and potentially the only element in a medical device subject to regulatory conformance. These regulations have created confusion surrounding specific areas such as the use of mobile device applications for healthcare purposes. This article describes the key points of these latest regulatory changes that medical device manufacturers need to be aware of.

Keywords: MDD 2007/47/EC, Medical Device Data System, MDDS, Software, Medi SPICE

Introduction

Failures in medical devices can have severe and fatal consequences [1, 2]. To prevent these failures from impacting on patient safety regulations were in place by competent authorities to ensure safe and reliable operation of medical devices. The international medical device regulatory environment is continually evolving and over the past two years there have significant regulations entered into

force. These regulations include the latest amendment to the Medical Device Directive 2007/47/EC [3] and the US Food and Drug Administration (FDA) Final Rule on Medical Device Data Systems (MDDS) [4]. These regulations are in response to the changing environment of medical devices utilisation. This is evident in the amended definition of a medical device as part of the amended MDD, where software has now been explicitly included. This is also evident in the MDDS regulation where certain mobile device applications used within healthcare are now subject to regulatory conformance. Both of these recent regulatory changes, the EU amendment to the MDD & FDA MDDS, provide clarity to specific areas, but unfortunately have also created a level of ambiguity in other areas of medical device development. The aim of this article is to provide clarity for medical device manufacturers and researchers on the application of these regulations to medical device development projects.

EU MDD 2007/47/EC

On March 21st 2010 the latest EU amendment to the MDD came into force [5]. This amendment marks the fifth amendment to the original directive 93/42/EEC [6]. It also amends the Active Implantable Medical device (AIMD) directive 90/385/EEC [7] and the Biocides directive 98/8/EC [8]. Compliance to the current MDD is mandatory for a device manufacturer to be able to market a medical device for use within the EU. Unlike the US, there is no single authority in the EU which is responsible for ensuring compliance with regulatory standards. The EU compliance mark i.e. CE, is awarded by notified bodies within each member state of the EU. Once a CE mark has been awarded within a member state, a manufacturer is free to market their device in all EU member states [9]. As part of this latest amendment, there are major areas which have been amended which will impact on medical device manufacturers:

1. Clinical Data

Prior to the release of MDD 2007/47/EC clinical data was only required when seeking regulatory approval for Class IIa, Class IIb and Class III devices. However, this has now

changed and as a result clinical data must be supplied when seeking regulatory approval regardless of device classification. Clinical data is defined as *safety and/or performance information that is generated from the use of a medical device*.

2. *Retention of Record*

Medical device manufacturers must retain their records for inspection by competent authorities for either the useful life of the product or for five years, whichever length of time is greater.

3. *Class I device manufacturers may now choose Annex II Conformance Route*

As part of the latest MDD, guidance is provided as to what methods a manufacturer can use in order to achieve regulatory compliance. These methods are provided in the Annexes of the MDD. Prior to this amendment, manufacturers of Class I devices could not follow Annex II of the MDD to achieve regulatory approval. This has now been changed to now allow Class I device manufacturers the option of choosing the compliance method as part of Annex II.

4. *Outsourced design and manufacturing process to be monitored more closely*

Outsourcing is becoming increasingly common in all industries. As part of the latest MDD amendment, should a device manufacturer outsource any part of the design or manufacturing process, then the manufacturer must be able to demonstrate that adequate controls have been put in place to ensure the supplier is fully utilising a quality management system. Medi SPICE [10], a medical device software process assessment model is currently under development by the Regulated Software Research Group (RSRG) at Dundalk Institute of Technology (DkIT) and will be made available to the medical device industry. The results of a Medi SPICE assessment will indicate the capability of a software organisation to develop safe and reliable software. Therefore, assisting medical device manufacturers to ensure the reliability of software developed by third party suppliers for use as, or part of, a medical device.

5. *Design Documentation inspected more closely*

The primary function of the MDD is to provide guidance to device manufacturers regarding the development of safe, reliable medical devices in order to achieve regulatory compliance. However, specific elements of the MDD are targeted at notified bodies, with notified bodies now being required to perform inspections of design documentation for a representative sample of devices using industry standard statistical techniques, commensurate with the risk of the device.

6. *Authorised Representative explicitly noted*

Medical device manufacturers must appoint an authorised representative which can be contacted in lieu of the manufacturer. This is applicable to all devices regardless of classification.

7. *Software can now potentially be an active medical device*

The definition of a medical device has been amended to explicitly include software. Previous amendments did allow for software being a component of a medical device, but they did not include software being classified an active medical device in its own right. This can result in software being the only element of a medical device, and as such be subject to regulatory conformance [11]. As a safeguard, a caveat has been added to the MDD in Annex I Section 12a stating:

“For devices which incorporate software or which are medical software in themselves, the software must be validated according to the state of the art taking into account the principles of development lifecycle, risk management, validation and verification.”

The term “State of the Art” is used here to demonstrate what is generally accepted as good practice. Since this requirement was introduced, medical device software developers must now validate the software (integrated or standalone) regardless of device class.

8. *Post market surveillance applicable to custom devices*

Previously custom device manufacturers were not subject to post market surveillance by notified bodies. This has changed with the latest amendment and custom device manufacturers are now subject to post market surveillance.

9. Revision control of Instructions for use (IFU)

As part of the amendment, the date of issue of the latest IFU must be clearly indicated on the device.

10. Products deemed borderline

Devices that are deemed to border between a medical device and a medicinal product are determined based upon Primary mode of Action. Prior to this amendment this was determined by intended use.

11. Central circulatory system definition has been expanded

The definition of the central circulatory system has been expanded to include the vessels aortic arch and the descending aorta to the aorta bifurcation. Any device that comes in contact with these vessels is automatically considered Class III

12. Continuous use definition has been expanded

Prior to this amendment, continuous use applied to a single device for the length of time used until it is discontinued or replaced. However as part of the MDD if a device is immediately replaced by an identical device the period of use remains unbroken and the use is deemed continuous.

13. European databank to be established

MDD 2007/47/EC mandates the establishment of a European Databank. The databank is to contain data related to clinical investigations, information on registration, authorised representative, certificates and vigilance data. This databank will be accessible to all notified bodies and must be operational by September 2012.

14. Human tissue

Devices that incorporate human blood, tissue or plasma which fall within the scope of Medicinal Products for Human Use directive 2001/83/EC are automatically considered Class III devices.

US FDA Rule on MDDS

On April 16th 2011 the FDA released its final rule concerning MDDS. As part of this rule the definition of a MDDS is provided:

“a device that is intended to provide one or more of the following uses, without controlling or altering the functions or parameters of any connected medical device:

- (i) The electronic transfer of medical device data;*
- (ii) The electronic storage of medical device data;*
- (iii) The electronic conversion of medical device data from one format to another format in accordance with a pre-set specification;*
- (iv) The electronic display of medical device data.”*

Prior to the release of this rule, a device that performed any of the above functions automatically received a Class III safety classification as defined by the Federal Food, Drug and Cosmetics Act or received the safety classification of the parent device to which they are connected until the manufacturer applies to the FDA for device reclassification. With the release of this rule, a device that solely performs one or more of the above functions now receives a Class I safety classification.

Whilst a primary goal of this ruling is to streamline the process of achieving regulatory approval for devices that meet the definition of being a MDDS, confusion has arisen surrounding a number of areas relating to this rule such as the definition of medical device data, active patient monitoring, medical device data translation, mobile device software and items beyond the scope of the MDDS classification [12].

Medical Device Data

Medical device data is considered as either data that is obtained directly by a medical device for electronic transfer or clinical data inputted manually which is intended for electronic transfer. For example, if a clinician enters a patient's test results into a computer for storage that data is not considered medical device data as it is not intended for electronic transmission. Conversely if a blood pressure monitor stores information and transfers that information then that information is deemed medical device data.

Active Patient Monitoring

A device is deemed to perform active patient monitoring if the information obtained from a medical device is utilised to perform immediate corrective action with regard to patient safety. Devices that perform active patient monitoring fall beyond the scope of being a MDDS. These devices remain classified as Class III devices (until reclassified by the FDA) or as accessories to the medical devices to which they are connected and consequently inherit the safety classification of the device to which they are connected. For example, a medical device that triggers an alarm to notify clinicians of a change in a patient's condition is not a MDDS and is subject to separate regulatory scrutiny.

Medical device data translation

An area which creates a level of confusion amongst medical device manufacturers is devices which perform medical device data translation and whether or not these devices are deemed to meet the requirements of being a MDDS. As part of the MDDS ruling a device is deemed a MDDS if it translates medical device data, but does not alter that data in any way. For example a MDDS device may translate Health Level 7 (HL7) information into a spread sheet format. The definition of a MDDS explicitly mentions that a MDDS cannot alter the function of a medical device to which it is connected or the data that is being transmitted.

Mobile Device Software

The usage of mobile devices within healthcare is increasing. The number of mobile applications which can be utilised within healthcare is growing exponentially. An example of such software is Medscape, a medical application designed to run on the Apple iPhone. Previously, medical software application developers were avoiding regulatory scrutiny by stating that their applications were not intended for active patient monitoring or for any of the functions defined as being a MDDS. However with the release of the MDDS final rule, certain mobile applications are within the scope of being a MDDS, if they perform one or more of the functions as defined in the MDDS definition.

Beyond the scope of the MDDS classification

As part of this ruling, a number of devices used within healthcare would appear to meet the definition of being a MDDS, but are excluded from the MDDS classification for varying reasons. For example, hospital network infrastructure devices such as network routers and hubs are not subject to regulatory scrutiny as they were not specifically developed for use in a healthcare environment to transfer patient information.

Software applications such as Electronic Health Records (EHR) and Computerised Physician Order Entry (CPOE) also fall beyond the scope of a MDDS [13]. Whilst these software applications would appear to perform the functions as defined by the MDDS definition, they have been excluded from the ruling as it is envisaged that these software applications will, in the future, be able to automatically order patient tests. This will lead to the automatic generation of medical device data and this is explicitly beyond the scope of the MDDS definition.

Medical device alarms fall beyond the scope of being a MDDS. Alarms connected to medical devices possess the ability to inform clinicians that immediate corrective action regarding a patient's well-being is required. This would be deemed as performing the function of active patient monitoring and the alarm would be defined as an accessory to the parent medical device. Consequently, alarms connected to devices that are classified as being MDDS are deemed as being

MDDS as they only monitor the condition of the MDDS to which they are connected and do not monitor a patient's condition.

What Next?

As technology used within healthcare continually evolves the regulations and standards associated with that technology need also to evolve. The current life-cycle standard followed by medical device software developers is IEC 62304:2006 Medical Device Software Life-cycle Processes [14]. IEC 62304 is a harmonised standard as part of the MDD [15]. The most recent version of IEC 62304 was released in 2006, prior to the release of the latest amendment to the MDD. Consequently, it does not provide sufficient guidance in the development of standalone medical device software to meet the requirements of the MDD. However, IEC 82304 Healthcare Software Systems, is currently under development and is expected to provide guidance in the development of all types of medical device software including standalone software.

As mentioned previously, EHR and CPOE have been explicitly excluded from the scope of a MDDS. To remove the ambiguity surrounding EHR, CPOE and certain mobile applications the FDA began drafting a guidance document in July 2010. On July 21st 2011 the FDA released its Draft Guidance for Industry and Food and Drug Administration staff – Mobile Medical Applications [16]. This document has been issued to explain the FDA intentions to apply its regulatory requirements to a subset of mobile applications.

The FDA MDDS ruling only applies to medical devices marketed for use in the US. However the European Council has, however recognised the need for a comparable ruling that can be applied to the EU market. The European Council convened a meeting of the Medical Expert Group late last year. The objective of this meeting was to discuss the need for regulation regarding what the FDA defines as being a MDDS and the classification of different types of software used within healthcare. As a result of this meeting a MED DEV guidance document [17] has been released in January. This MED DEV document provides clarity as to what categories the various types of software used in healthcare fall into.

Summary

As the medical device international regulatory environment is continually evolving medical device developers need to be aware of recent and upcoming regulatory changes. Developing a medical device can be a lengthy process. The regulatory environment at the beginning of a development project can be very different to that which is in place when the device is being marketed. The latest FDA MDDS ruling improved the process of achieving regulatory compliance for a number of medical device manufacturers, but unfortunately a level of ambiguity has arisen regarding areas such as active patient monitoring and medical data translation. The MDD 2007/47/EC has also made a number of significant amendments to the original directive 93/42/EEC that directly impacts the development of medical devices. Understanding these changes can greatly improve a medical device manufacturer's process of achieving regulatory approval.

Acknowledgments

This research is supported by the Science Foundation Ireland (SFI) Stokes Lectureship Programme, grant number 07/SK/I1299, the SFI Principal Investigator Programme, grant number 08/IN.1/I2030 (the funding of this project was awarded by Science Foundation Ireland under a co-funding initiative by the Irish Government and European Regional Development Fund), and supported in part by Lero - the Irish Software Engineering Research Centre (<http://www.lero.ie>) grant 10/CE/I1855

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